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10/081,563	02/22/2002	David M. Herrington	9151-15	2002

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EXAMINER

SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/081,563		Applicant(s) HERRINGTON ET AL.	
	Examiner Bradley L. Sisson		Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on ____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-23 is/are pending in the application.

4a) Of the above claim(s) 3-23 is/are withdrawn from consideration.

5) ☐ Claim(s) ____ is/are allowed.

6) ☒ Claim(s) 1 and 2 is/are rejected.

7) ☐ Claim(s) ____ is/are objected to.

8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. ____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.

4) ☐ Interview Summary (PTO-413) Paper No(s). ____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1 and 2, drawn to a method of screening a subject for an increased likelihood of having a favorable response to estrogen replacement therapy with respect to cardiovascular health, classified in class 436, subclass 501.
 - II. Claims 3-7, drawn to a method of decreasing the risk of heart disease, classified in class 514, subclass 2.
 - III. Claims 8-12, drawn to a method of treating a subject for depressed ADL levels, classified in class 514, subclass 2.
 - IV. Claim 13, drawn to an isolated nucleic acid encoding the human estrogen receptor alpha comprising IVS1-1415 polymorphism, classified in class 536, subclass 23.5; claim 14, drawn to an oligonucleotide that specifically binds to an isolated nucleic acid encoding human estrogen alpha comprising IVS1-1415 polymorphism, classified in class 536, subclass 24.31; claim 15, drawn to a vector, classified in class 435, subclass 320.1; and claim 16, drawn to a host cell, classified in class 435, subclass 252.3.
 - V. Claim 17, drawn to isolated nucleic acid encoding the human estrogen receptor alpha comprising IVS1-1505, classified in class 536, subclass 23.5; claim 18, drawn to an oligonucleotide that specifically binds to an isolated nucleic acid encoding the human estrogen receptor alpha comprising IVS1-1505; claim 19,

drawn to a vector, classified in class 435, subclass 320.1; and claim 20, drawn to a host cell, classified in class 435, subclass 252.3.

VI. Claim 21-23, drawn to a method of conducting a clinical trial on a plurality of human patients, classified in class 514, subclass 2.

2. The inventions are distinct, each from the other because of the following reasons:

3. Inventions I, II, III, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are all drawn to different methods that have different modes of operation and effects.

4. Inventions IV and V are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention of Group IV has separate utility such as production of an immunogen. See MPEP § 806.05(d).

5. Inventions IV and V, and I-III and IV are related as products (IV and V) and processes of use (I-III and VI). The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products can be used in any of the other methods.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Jarrett K. Abramson, Reg. No. 47,376, on 23 July 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1 and 2. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-23 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

9. The disclosure is objected to because of the following informalities: At page 2, paragraph 10, line 5, unmatched parenthesis are found. Additionally, at page 2, last line "aboveabove" is noted.

Appropriate correction is required.

10. The specification is objected to as documents have been improperly incorporated by reference, e.g., US Patents at paragraphs 32 and 43. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USPQ 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application.**) (Emphasis added.)

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

13. As presently worded, the method of claims 1 and 2 is to result in the identification of those individuals that are to have “a favorable response to estrogen replacement therapy with respect to cardiovascular health.” For purposes of examination, the phrase has been interpreted as encompassing angiographically defined coronary disease. Additionally, the term “subject” has been interpreted as encompassing all life forms that have a heart.

14. A review of the disclosure finds support for the position that women that have the IVS1-354 polymorphism, the IVS1-401 polymorphism, the IVS1-1415 polymorphism, and the IVS1-1505 polymorphism and which received hormone replacement therapy had an increase in HDL levels. The specification is essentially silent as to any of these increases in HDL being correlated with a favorable response in cardiovascular health.

15. In support of this position, attention is directed to page 17, paragraph 70, which states in part:

Despite the favorable effects on HDL levels, progression of angiographically defined coronary disease was not significantly different among women with the IVS1-401 C/C genotype on HRT compared to the other women assigned HRT; although, the power to detect such an interaction for the angiographic endpoint was extremely limited. None of the other *ER-α* polymorphisms examined, including several different classifications of the promoter TA repeat, was associated with change in HDL cholesterol in response to HRT.

16. The specification has not presented any evidence that the presence of these polymorphisms are found in other life forms, and that any of them has been shown to correlate with improved cardiovascular disease in women, much less men and other life forms.

While there is no per se rule that the claimed invention must be enabled via examples, it is well settled that the level of disclosure required varies inversely with the predictability in the art. The claimed invention relates directly to matters of physiology and chemistry, which are

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inherently unpredictable and as such, require greater levels of enablement. As noted in *In re*

Fisher 166 USPQ 18 (CCPA, 1970):

In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

17. It is clear that the claimed invention relates to issues of both chemistry and matters of physiology and the prediction of future physiological phenomena- cardiovascular disease. The record also clearly states that the presence of the claimed polymorphisms, even when it results in an increase in HDL, did not correlate with a significant difference in coronary disease.

In view of the breadth of scope claimed, the limited guidance provided, the unpredictable nature of the art to which the claimed invention is directed, and in the absence of convincing evidence to the contrary, the claims are not enabled by the disclosure.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Said claims are indefinite with respect to what constitutes "a favorable response to estrogen replacement therapy with respect to cardiovascular health."

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Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is 703-308-3978.

The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5 PM.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

22. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
July 25, 2003